Astoria-Pacific™
INTERNATIONAL

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Summary, 510(k) No. k080294

1. Name, Address of Contact Person and Date of Preparation

Applicants name and address

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Official Correspondent
Director of Research & Development

Signature of Applicant:
Date: October 23, 2008

Jason Reynolds

Jason Reynolds

2. Name of the Device

Product Classification

Regulation Number	21 CFR 862.1118
510(k) Number	K080294
Classification Panel	Clinical Chemistry
Product Code	NAK
Device Classification	Class II

Product Nomenclature

Common Name	Biotinidase Screening Test
Classification Name	Biotinidase Test System
Proprietary Name	Astoria-Pacific SPOTCHECK® Biotinidase Microplate Reagent Kit
Model Number	Astoria-Pacific Part No. 81-8000-13K

3. Identification of the legally-marketed device for which substantial equivalence is claimed

Product Classification

Regulation Number	21 CFR 862.1118
510(k) Number	K010844
Classification Panel	Clinical Chemistry
Product Code	NAK
Device Classification	Class II

Product Nomenclature

Common Name	Biotinidase Screening Test
Classification Name	Biotinidase Test System
Proprietary Name	Astoria-Pacific SPOTCHECK Biotinidase Kit, 50-Hour
Model Numbers	Astoria-Pacific Part Number 80-8000-13K

4. Description of the Device

SPOTCHECK Biotinidase Microplate Reagent Kit

API Part No. 81-8000-13K
Biotinidase Test System

KIT CONTENTS:

Color Reagent 1
Color Reagent 1 Diluent
Color Reagent 2
Color Reagent 2 Diluent
Color Reagent 3
Substrate
Substrate Diluent
Substrate Buffer
Stock Standard
Trichloroacetic acid (TCA)

Biotinidase activity is determined by measuring the color that develops from p-Aminobenzoic Acid (PABA) after PABA is released from Biotinyl-p-Aminobenzoate (Biotin-PAB). Samples with biotinidase activity develop a purple color. Samples without biotinidase activity remain straw-colored.

Patient samples of whole blood collected on standardized filter paper are eluted in a standard 96 well microplate. The plate is incubated with Biotin-PAB in a buffer at 37°C for 240 minutes on a combination incubator/shaker. Following incubation, TCA is added to the sample mixture and the resulting precipitate is

removed through filtration. The PABA in the filtrate is subsequently diazotized and coupled to a napthol derivative to form an azo dye by the successive addition of sodium nitrite, acidic ammonium sulfamate and finally, N-1-naphthylethylenediamine dihydrochloride (NED). The azo dye is measured colorimetrically at 550 nm on a commercial microplate absorbance reader with a reference measurement at 690 nm.

$$\text{Biotin-PAB} \xrightarrow{\text{Biotinidase}} \text{Biotin} + \text{PABA}$$

$$\text{PABA} \xrightarrow[\text{NED}]{NO_2,\ NH_2SO_3} \text{Purple chromophore}$$

The color developed is proportional to the biotinidase activity in the sample. A standard curve prepared from a stock PABA solution is used to evaluate the results.

5. Statement of Intended Use

This method is for the semi-quantitative determination of biotinidase, EC 3.5.1.12, activity in dried whole blood spots using a spectrophotometer. Measurement of biotinidase activity is primarily for the diagnosis and treatment of biotinidase deficiency in newborns. This method is intended for in vitro diagnostic use to aid in screening for decreased levels of biotinidase activity and not for monitoring purposes.

This device is for use by trained, qualified laboratory personnel.

6. Summary of the Technological Characteristics of the Device

DEVICE COMPARISON

The most significant difference between the SPOTCHECK Biotinidase Microplate Reagent Kit and the predicate device is the intended analyzer platform. The predicate device is used on a segmented-flow analyzer while the new reagent kit is for manual laboratory use only, applying simple bench chemistry techniques (e.g. pipetting) and utilizing a combination incubator/shaker and spectrophotometric microplate reader. The units used for the two assay kits are also different: microplate response units (MRU) for the new kit and enzyme response units (ERU) for the predicate device (1 MRU $\neq$ 1 ERU).

Newborn patient blood spots are punched into microplate wells, eluted and incubated with the same substrate and buffer system as on the predicate device. Extraction and incubation occur concurrently, whereas on the predicate device, samples are first eluted, then vacuum filtered and subsequently incubated on the analyzer system. The predicate device utilizes automated dialysis to remove interferences. The SPOTCHECK Biotinidase Microplate Reagent Kit however, uses a reagent not included with the predicate device to precipitate matrix interferences which are subsequently removed through vacuum filtration. The same reagent formulation is used on both devices to generate the azo dye measured at 550 nm.

Summary of Predicate Device and Microplate Kit Technological Characteristics

	SPOTCHECK Biotinidase Microplate Reagent Kit	*Predicate Device*
Sample collection and handling	Use standardized filter paper, S&S®903™ Follow CLSI document LA4-A5: *Blood Collection on Filter Paper for Newborn Screening*	Same collection and handling
Sample	2 x 1/8" punched blood spot	Same patient sampling
Incubation	In microplate, on combination incubator/shaker	On flow analyzer system
Matrix interference mitigation	Chemical precipitation and manual vacuum filtration	Manual vacuum filtration and dialysis on the flow analyzer system
Incubation Temp	37°C	40°C
Incubation Time	240 minutes	~120 minutes
Color Reagents	Sodium nitrite, acidic ammonium sulfate, NED	Same formulation
Incubation substrate	Buffered Biotinyl-p-Aminobenzoate	Same formulation
Absorbance measurements	Spectrophotometric microplate reader - 550 nm (reference at 690 nm)	Flow through split-beam spectrophotometer - 550 nm
Units of measurement	Microplate response unit (MRU) 1 MRU equals 1 µmol of p-aminobenzoic acid produced from Biotin-PAB per dL per 240 minutes of incubation at 37°C	Enzyme response unit (ERU) 1 ERU defined as the azo dye formed from 1 µmol of p-aminobenzoic acid produced from Biotin-PAB per dL per ~120 min. of incubation at 40°C
Deficient cutoff	10% mean activity of population	Same cutoff
Partial Activity cutoff – Clinical decision level	37% mean activity of population	Same cutoff

LINEARITY

Calibration standards are analyzed at the beginning of each assay using the SPOTCHECK Biotinidase Microplate Kit, as with the predicate device. The calibration utilizing PABA standards ranges from 0 to 200 MRU with a typical correlation coefficient of at least 0.999. Additionally, the assay was deemed linear after evaluation over the range of 5 to 213 MRU adhering to CLSI EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.*

SENSITIVITY

The Limit of Blank (LoB) and Limit of Detection (LoD) for biotinidase activity are 2 and 3 MRU, respectively, determined using the guidelines in the CLSI EP17-A protocol. The total error is less than the LoD, and the CLSI document prescribes that the Limit of Quantitation (LoQ) is equal to the LoD. This correlates well with the sensitivity of the predicate device.

DETERMINATION of CLINICAL CUTOFF

The recommendation for determining the clinical action cutoff and cutoff for profound deficiency are the same for both devices: 37 and 10% of the mean patient result, respectively. As with the predicate device, each laboratory must determine its range of normal, partial and deficient levels of biotinidase activity, based on its population and analytical variables. All samples below the partial activity cutoff require follow-up screening according to local, state and federal laws.

CLASSIFICATION of DEFICIENT and UNCLASSIFIED PATIENT SAMPLES

The performance of the SPOTCHECK Biotinidase Microplate Reagent Kit was evaluated against the predicate device by analyzing unclassified (564) and biotinidase deficient (2) patient samples and (10) deficient controls provided by the Centers for Disease Control (CDC). All deficient patient samples are from persons clinically-confirmed as such. Samples analyzed with the SPOTCHECK Biotinidase Microplate Reagent Kit were treated according to the procedures detailed under SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS in the product insert.

Classification of Samples during Device Comparison

		Predicate device		
		Deficient	Partial Activity	Normal
Microplate Kit	Deficient	11 of 11	0	0
	Partial Activity	0	4 of 5*	1**
	Normal	0	1**	559 of 560

Note: 1 partial* and the 11 deficient represent the 2 clinically-confirmed patients and 10 CDC deficient controls. Discrepant results ** were not confirmed by follow-up testing.

PRECISION

To evaluate within-run and total precision (according to CLSI Document EP5-A2) for the new device, Astoria-Pacific's Quality Assurance Laboratory completed 2 analyses per day, of samples in duplicate, for 20 days. An additional low-activity precision study was performed over 5-days only on the Microplate Kit. A summary of the data is shown below compared to the historical performance evaluation of the predicate device. The predicate device evaluation utilized data from 2 runs per day for 8 days (deficient) to 11 days (normal and near deficient) according to NCCLS Document EP5-T.

Within-Run Precision, S_{WR}

SPOTCHECK Biotinidase Microplate Reagent Kit

Biotinidase Activity, MRU	Low Activity n = 80	Moderate Activity n = 80	Normal n = 80
Average	18.3	50.7	124.9
S.D.	1.2	2.2	4.7
C.V.	6.3%	4.4%	3.8%

Predicate Device

Biotinidase Activity, ERU	Low Activity n = 32	Moderate Activity n = 44	Normal n = 44
Average	0.54	14.6	79.6
S.D.	0.09	0.47	3.8
C.V.	17%	3.2%	4.7%

Total Precision, S_T

SPOTCHECK Biotinidase Microplate Reagent Kit

Biotinidase Activity, MRU	Low Activity n = 80	Moderate Activity n = 80	Normal n = 80
Average	18.3	50.7	124.9
S.D.	1.7	3.7	8.9
C.V.	9.4%	7.3%	7.1%

Predicate Device

Biotinidase Activity, ERU	Low Activity n = 32	Moderate Activity n = 44	Normal n = 44
Average	0.54	14.6	79.6
S.D.	0.30	0.94	4.5
C.V.	56%	6.4%	5.8%

Additional 5-day study results

SPOTCHECK Biotinidase Microplate Reagent Kit

Mean Biotinidase Activity, MRU (n = 80)	10.3
S_r (within-run precision)	0.6
C.V. (within-run)	5.8%
B (daily mean precision)	0.8
S_T (total precision)	1.1
C.V. (total)	9.7%

The SPOTCHECK Biotinidase Microplate Reagent Kit is effective at screening out patient samples deficient in biotinidase activity. The precision is comparable and in some cases, greatly improved.

INTERFERING SUBSTANCES

No known significant differences that would affect safety and effectiveness were observed when compared to the predicate device during the evaluation of interfering substances. The SPOTCHECK Biotinidase Microplate Reagent Kit was evaluated according to CLSI EP7-A2: *Interference Testing in Clinical Chemistry; Approved Guideline.* A summary of the findings and comparison to the predicate device is presented below.

Interference Evaluated	***SPOTCHECK Biotinidase Microplate Reagent Kit***	***Predicate Device***
Sulfonamides[1]	1.58 mmol/L (400 µg/mL) sulfamethoxazole has a clinically significant effect on biotinidase activity classification – patients treated with sulfonamides should be screened using an alternate method	No limit established, but a known interference is cited

Albumin	albumin concentrations above normal can show positive interference of 1.6 MRU per 1 g/dL albumin	25 g/L albumin showed no interference; > 25 g/L effected significant interference
Hemoglobin	2 g/L hemoglobin caused no clinically significant interference	1 g/L hemoglobin caused no clinically significant interference
Lipids	37 mmol/L (3270 mg/dL) lipids caused a decrease in response; may cause false positives – no risk to deficient patients	2.5 g/L lipids showed no clinically significant interference
Bilirubin	342 µmol/L *direct* (conjugated) or *indirect* (unconjugated) bilirubin (~0.3 and ~0.2 g/L, respectively) caused no clinically significant interference	0.25 g/L bilirubin showed no interference
Trimethoprim	138 µmol/L (40 µg/mL) trimethoprim caused a decrease in response; may cause false positives – no risk to deficient patients	No limit established
Gamma globulin	60 g/L gamma globulin caused no clinically significant intereference	No limit established

Phenytoin, ampicillin, gentamicyn sulfate, vitamin K, penicillin G potassium, kanamycin sulfate, adrenocorticotropic hormone, valproic acid and sodium phenobarbital do not interfere at therapeutic concentrations.[1,2]

7. Determination of Substantial Equivalency

Based on performance characteristics and comparison data, we believe this device to be safe, effective, and substantially equivalent to the legally-marketed predicate device. The indications for use are the same for the SPOTCHECK Biotinidase Microplate Reagent Kit and the predicate device. Technological characteristics are very similar to the predicate device and there is sufficient evidence demonstrating that the differences do not significantly affect safety and effectiveness when analyzing clinical patients.

1. Gregory S. Heard, J. S. McVoy and B. Wolf, *A Screening Method for Biotinidase Deficiency in Newborns*, Clinical Chemistry, **30**, 125-127, 1984.
2. Barry Wolf, G. S. Heard, K. A. Weissbecker, J. R. Secor McVoy, R. E. Grier and R. T. Leshner, *Biotinidase Deficiency: Initial Clinical Features and Rapid Diagnosis*, Annals of Neurology, **18**, 614-617, 1985.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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NOV - 4 2008

Re: k080294

Trade/Device Name: Spotcheck Biotinidase Microplate Reagent Kit
Regulation Number: 21 CFR 862.1118
Regulation Name: Biotinidase test system
Regulatory Class: Class II
Product Code: NAK
Dated: October 23, 2008
Received: October 27, 2008

Dear Mr. Reynolds:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0490. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

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Director
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Office of *In Vitro* Diagnostic Device
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Enclosure

INDICATIONS FOR USE

510(k) K080294

SPOTCHECK® Biotinidase Microplate Reagent Kit

INTENDED USE

This method is for the semi-quantitative determination of biotinidase, EC 3.5.1.12, activity in dried whole blood spots using a spectrophotometer. Measurement of biotinidase activity is primarily for the diagnosis and treatment of biotinidase deficiency in newborns. This method is intended for in vitro diagnostic use in screening for decreased levels of biotinidase activity and not for monitoring purposes.

This device is for use by trained, qualified clinical laboratory personnel.

Prescription Use __X__ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Carol C. Benson

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K080294